REMARKS

In response to the Office Action mailed July 17, 2001, claims 14, 15, and 34 have been amended. Just as the Office has previously withdrawn its first requirement for restriction by paper mailed March 22, 2001, Applicant withdraws his election, which was made without traverse pursuant to paper filed April 23, 2001. In this paper, pursuant to MPEP §818.03(c), Applicant respectfully traverses and requests reconsideration of the imposed requirement for restriction.

Election has been required under 35 USC § 121 to the follow five (previously four) separate groups:

I. Claims 1-13, drawn to laser capture microdissection process wherein an activatable layer is caused to volumetrically expand, classified in class 435, subclass 30, for example.

II. Claims 14 to 15, drawn to laser capture microdissection process wherein an activatable layer is caused to differentially, volumetrically expand, classified in class 436, subclass 63. (emphasis added).

III Claims 16 to 28, drawn to apparatus for non-contact laser capture microdissection, classified in class 422, subclass 101, for example.

IV. Claims 29 to 33, drawn to process of making a surface for non-contact laser microdissection, classified in class 436, subclass [not specified], for example.

V. Claims 34 to 46, drawn to laser capture microdissection process wherein an activatable layer is provided with a support substrate and is caused to volumetrically expand, classified in class 435, subclass 40.5, for example. (In the original requirement for restriction this was included in Group I)

Pursuant to the requirement of 37 CFR 1.143, Applicant elects Group I, with traverse. Specifically, Applicant traverses the requirement for separate examination of Groups I, II, and V.

First, with respect to Groups I and II, as can be seen the emphasized portion of the restatement of the requirement, the only difference between the claimed process is expansion compared to differential expansion. In imposing the requirement, the examiner has made the statement:

> ...The subcombinations are distinct from each other if they are shown to be separately usable. In the instant case, Invention I has separate utility wherein the laser capture microdissection process is used for capturing biomaterials into microbeads for use in solid phase assays[1]. See MPEP § 806.05(d)

Second, and in response to the last sentence of MPEP § 806.05(d), these inventions are now the subject of amended claims. Claims 14 and 15 now depend from claim 1. The are now generically claimed. Further, Applicant traverses the Examiners statement that these inventions can be "separately used." As can be seen, differential expansion is a specie of expansion. The statement made in support of the requirement for restriction fails to show how capturing biomaterials into microbeads for use in solid phase assays is any different under differential expansion as it is under just plain expansion

Third, the requirement ignores the definition of "distinct." Referring to MPEP 802.01 **Meaning of "Independent" and "Distinct"**, "distinct" is defined as:

> The term "distinct" means .... but are capable of separate manufacture, use or sale as claimed, AND ARE

[1] The Examiner uses the statement, "the laser capture microdissection process is used for capturing biomaterials into microbeads for use in solid phase assays" six times in this Requirement for Restriction. Applicant respectfully requests that art be cited representative of this statement so that the record herein may be complete.

PATENTABLE (novel and unobvious) OVER EACH OTHER ....(Emphasis by CAPITAL LETTERS not added; the authors of the MPEP intended the capitalization).

Additionally, the statement is made on page 6 of the requirement, "Furthermore, because the search required for Group I is not required for Group II,..." This invention relates to expansion in **film**. The claims make it clear that the expansion is **normal** to the film. How one would have to search different areas because expansion normal to the film is "differential" in one case and not "differential" in another case is not seen.

Laser capture microdissection essentially started with the invention claimed and set forth in Liotta et al. US Patent 5,843,657 issued December 1, 1998. Applicant's attorney issued this patent and continues to prosecute Divisional Applications from that original filing. The art simply has not progressed to the point where additional and substantial searching is required where "differential expansion" is claimed over regular "expansion."

It is therefore respectfully requested that this requirement be withdrawn.

Applicant also respectfully traverses the restriction between Groups I and V, this latter requirement being imposed for the first time in this second requirement for restriction.

In traversing this requirement, Applicant sets forth claim 34. First, argument is made in view of the recent origin of this art that the processes claimed are not "distinct" in that they are not patentable over one another. Second, and with respect to claim 34, it will be demonstrated that each and every element of that claim is included in the format of Group I in the dependent claims. This being the case, it is not seen how separate search is required.

First, the premise of Claim Groups I and V is the same. Laser capture microdissection film is held overlying a specimen, a very short distance from the specimen. When it is heated, the film expands across the very short distance, contacts, and adheres to the specimen. This enables the laser capture microdissection.

So how does the process of Group I differ from the process of Group V?

It is instructive to look at the text of claim 34, and note the claim correspondence to the claims of Group I. From this it can be seen, the respective art areas are so close that neither invention is non-obvious in view of the other (See MPEP 802.01) nor requires substantial additional search.

First, for the convenience of the reader, claim 34 of Group V is repeated here with claim correspondence to claim of Group I noted in brackets.

> 34. (Once Amended) A method for non-contact laser capture microdissection from a visualized specimen, the method comprising the steps of:
>
> providing a support for supporting and viewing the visualized specimen; [See Group I, claim 3, the specimen there recited without the support; but how else can one see a specimen without a support?]
>
> providing a supporting substrate;[See Group I, claim 2]
>
> placing a selectively activatable layer on the supporting substrate, which upon activation causes volumetric expansion with an extremity of the volumetric expansion exceeding a first interval taken substantially normal to a surface of the selectively activatable layer; [See Group I, claim 2]
>
> interconnecting the supporting substrate and the support to maintain the first surface at a spatial separation from all parts of the visualized specimen in juxtaposition with respect to the visualized specimen at the first interval of spatial separation from the visualized specimen; and, [See the placing step in claim I]

locally activating the selectively activatable layer to bring the first surface into contact with the visualized specimen.[See the selectively activating step of claim 1].

In applying the requirement for restriction between Groups I and V, and Groups II and V, the Examiner states that the inventions are related as combination and subcombination. The Examiner admits in page 4, first full paragraph of the Action, that to sustain this restriction, it must be shown that "and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c))."

First, Applicant has amended the claim language of claim 34 by deleting what is believed to be an unnecessary limitation. This limitation may well have caused confusion to the Examiner, for which Applicant solicits the Examiner's pardon.

Second, observing claim 34, it virtually incorporates in differing claim language limitations found throughout the claims of Group I. How one could practically use the combination of claim 1 separately from the combination of claim 34 is not seen. Specifically, specimens as a practical matter have to be supported. Mounting [expandable] layers or anything else to a "supporting substrate" does not have sufficient differentiation to render the two process "distinct" within the meaning of MPEP 802.01.

Applicant submits that 35 USC § 121 should be administered with reason and discretion. The definition of "distinct" in terms of non-obvious is placed in MPEP 802.01 to assure reasonableness. Further, in an art area (laser capture microdissection) originating with Liotta et al. US Patent 5,843,657 issued December 1, 1998, searching of art areas is reasonably limited to readily identifiable art. Undue burden is not present.

For the information of the Examiner, the technology herein is being licensed by the United State government and exploited with published success by the National Institutes of Health. To impose prolix filing fees on virtually the same invention expressed in claim language having slight variation is burdensome to this public effort.

Applicant further objects to the imposed requirement for restriction as being prolix. Reasonable discretion should be used in the imposition of this requirement

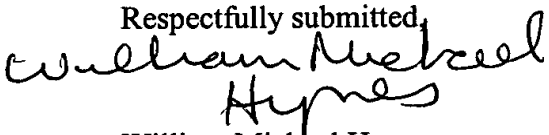
of the statute. It is submitted that the requirement for restriction separating Groups I, II, and V should be withdrawn. Action to that end is earnestly solicited.

CONCLUSION

In view of the foregoing, Applicants believe the restriction requirement separating Groups I, II, and V should be withdrawn.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



William Michael Hynes
Reg. No. 24,168

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: (415) 576-0200
Fax: (415) 576-0300
WMH
SF 1271985 v1

VERSION WITH MARKINGS TO SHOW CHANGES MADE

14. (Once Amended) A process of laser capture microdissection from a specimen according to claim 1 wherein the step of selectively activating the ~~[having the steps of:~~

~~providing a]~~ selectively activatable layer ~~[which upon activation by laser causes]~~ to cause volumetric expansion includes: ~~[upon heating;~~

~~placing the selectively activatable layer overlying the specimen at a separation less than a first interval;]~~

heating and expanding the selectively activatable layer to cause volumetric expansion first by locally heating and expanding a first inner volume of the selectively activatable layer with a component of expansion normal to the selectively activatable layer; and,

heating and expanding a surrounding second volume of the selectively activatable layer with a component of expansion in a plane of the selectively activatable layer into the first volume whereby a total volumetric expansion occurs with the second volume expanding into and extruding the first volume for a total expansion at least to the first interval to locally contact a portion of the specimen at the extremity of the volumetric expansion.

15. (Once Amended) A process of laser capture microdissection from a specimen according to claim 14 ~~[having the steps of:]~~wherein the step of selectively activating the selectively activatable layer to cause volumetric expansion includes

the heating and expanding of the first inner volume includes generating or expanding a vapor bubble.

34. (Once Amended) A method for non-contact laser capture microdissection from a visualized specimen, the method comprising the steps of:

providing a support for supporting and viewing the visualized specimen;

providing a supporting substrate;

placing a selectively activatable layer on the supporting substrate, which upon activation causes volumetric expansion with an extremity of the volumetric expansion exceeding a first interval taken substantially normal to a surface of the selectively activatable layer;

~~[placing at least a first surface on the selectively activatable layer or contact with the visualized specimen;~~

~~]~~interconnecting the supporting substrate and the support to maintain the first surface at a spatial separation from all parts of the visualized specimen in juxtaposition with respect to the visualized specimen at the first interval of spatial separation from the visualized specimen; and,

locally activating the selectively activatable layer to bring the first surface into contact with the visualized specimen.

Claim Groups (As Amended)

Group I

1. A process of laser capture microdissection from a specimen having the steps of:

providing a selectively activatable layer which upon activation causes volumetric expansion with an extremity of the volumetric expansion exceeding a first interval taken substantially normal to a surface of the selectively activatable layer;

placing the selectively activatable layer overlying the specimen at a finite separation less than the first interval; and,

selectively activating the selectively activatable layer to cause volumetric expansion at least to the first interval to locally contact a portion of the specimen at the extremity of the volumetric expansion.

2. A process of laser capture microdissection from a specimen according to claim 1 having the steps of:

providing a supporting substrate; and,

adhering the selectively activatable layer to the supporting substrate.

3. A process of laser capture microdissection from a specimen according to claim 1 having the steps of:

visualizing the specimen; and,

selectively activating the selectively activatable layer overlying the desired target within the visualized portion of the specimen.

4. A process of laser capture microdissection from a specimen according to claim 1 where the selectively activating step includes:

forming a mechanical bond with the targeted portion of the specimen.

5. A process of laser capture microdissection from a specimen according to claim 1 having the steps of:

placing a prepared surface on the selectively activatable layer exposed to the specimen, the prepared surface having an affinity specific bond with at least one component of the specimen; and,

selectively activating the selectively activatable layer to cause the prepared surface to contact the specimen and form affinity specific bonds with those components of the targeted specimen having the specific surface affinity defined by the prepared surface on the activatable layer.

6. A process of laser capture microdissection from a specimen according to claim 1 having the steps of:

repeating the selectively activating of different portions of the selectively activatable layer to cause corresponding contact and capture of different targeted elements within the specimen.

7. A process of laser capture microdissection from a specimen according to claim 6 having the steps of:

moving the selectively activatable layer with respect to the specimen to concentrate the series of captured elements on the activatable layer compared to their spacing within the specimen(s).

8. A process of laser capture microdissection from a specimen having the steps of:

providing a laser activated selectively activatable layer having which upon laser activation causes heat generated volumetric expansion and upon cooling elastically contracts, an extremity of the volumetric expansion exceeding a first interval taken substantially normal to a surface of the selectively activatable layer;

placing the selectively activatable layer overlying the specimen at a separation less than the first interval; and,

selectively activating with laser energy to heat the selectively activatable layer to cause volumetric expansion at least to the first interval to locally contact and bond to a portion of the specimen at the extremity of the volumetric expansion;

removing the laser activation; and,

allowing the volumetric expansion to cool.

9. A process of laser capture microdissection from a specimen according to claim 8 having the steps of:

the allowing the volumetric expansion to cool step causes the volumetric expansion to contract separating the targeted portion of the specimen from a remainder of the specimen and thereby microdissecting the portion of the specimen from a remainder of the specimen.

10. A process of laser capture microdissection from a specimen according to claim 8 having the steps of:

the allowing the volumetric expansion to cool step maintains attachment to the portion of the specimen while elastically tensioning the volumetric expansion of the activatable layer; and,

withdrawing the activatable layer from the specimen to separate the portion of the targeted specimen from the remainder of the specimen thereby microdissecting the portion of the specimen from a remainder of the specimen.

11. A process of laser capture microdissection from a specimen according to claim 10 where the withdrawing the activatable layer step includes:

elastically contracting the volumetric expansion to withdraw the portion of the specimen bonded to the volumetric expansion within the first interval whereby the portion of the specimen bonded to the volumetric expansion cannot contact underlying and remaining portions of the specimen when the activatable layer is maintained separate from the specimen by the first interval.

12. A process of laser capture microdissection from a specimen according to claim 8 having the steps of:

the activatable layer includes strong long chain thermoplastic polymers with a large volume change associated with phase transition.

13. A process of laser capture microdissection from a specimen according to claim 8 having the steps of:

the activatable layer is attached to a supporting substrate.

Group II

14. (Once Amended) A process of laser capture microdissection from a specimen according to claim 1 wherein the step of selectively activating the selectively activatable layer to cause volumetric expansion includes:

heating and expanding the selectively activatable layer to cause volumetric expansion first by locally heating and expanding a first inner volume of the selectively activatable layer with a component of expansion normal to the selectively activatable layer; and,

heating and expanding a surrounding second volume of the selectively activatable layer with a component of expansion in a plane of the selectively activatable layer into the first volume whereby a total volumetric expansion occurs with the second volume expanding into and extruding the first volume for a total expansion at least to the first interval to locally contact a portion of the specimen at the extremity of the volumetric expansion.

15. (Once Amended) A process of laser capture microdissection from a specimen according to claim 14 wherein the step of selectively activating the selectively activatable layer to cause volumetric expansion includes

the heating and expanding of the first inner volume includes generating or expanding a vapor bubble.

Group V

34. (Once Amended) A method for non-contact laser capture microdissection from a visualized specimen, the method comprising the steps of:

providing a support for supporting and viewing the visualized specimen;

providing a supporting substrate;

placing a selectively activatable layer on the supporting substrate, which upon activation causes volumetric expansion with an extremity of the volumetric expansion exceeding a first interval taken substantially normal to a surface of the selectively activatable layer;

interconnecting the supporting substrate and the support to maintain the first surface at a spatial separation from all parts of the visualized specimen in juxtaposition with respect to the visualized specimen at the first interval of spatial separation from the visualized specimen; and,

locally activating the selectively activatable layer to bring the first surface into contact with the visualized specimen.

35. A method for non-contact laser capture microdissection from a visualized specimen according to claim 34, the method comprising the steps of:

the selectively activatable layer on the supporting substrate has a large volumetric expansion associated with activation.

36. A method for non-contact laser capture microdissection from a visualized specimen according to claim 34, the method comprising the steps of:

activating the selectively activatable layer to bring the first surface into contact with the visualized specimen includes thermoplastic injection of polymer into voids of the tissue sample.

37. A method for non-contact laser capture microdissection from a visualized specimen according to claim 34, the method comprising the steps of:

placing at least a first surface on the selectively activatable layer for contact with the visualized specimen includes providing the first surface with specific tethers for linking to specific cells in the sample.

38. A method for non-contact laser capture microdissection from a visualized specimen according to claim 34, the method comprising the steps of:

placing at least a first surface on the selectively activatable layer for contact with the visualized specimen with a monolayer coating on the surface with high affinity specific bonds for target cells on the visualized specimen.

39. A method for non-contact laser capture microdissection from a visualized specimen according to claim 34, the method comprising the steps of:

placing a selectively activatable layer on the supporting substrate includes placing material having a linear thermal expansion coefficient.

40. A method for non-contact laser capture microdissection from a visualized specimen according to claim 34, the method comprising the steps of:

placing a selectively activatable layer on the supporting substrate includes a material confining local expansion to an internally confined zone on all sides excepting the visualized specimen.

41. A method for non-contact laser capture microdissection from a visualized specimen according to claim 34, the method comprising the steps of:

placing a selectively activatable layer on the supporting substrate includes enclosing at least one air bubble within the selectively activatable layer.

42. A method of laser capture microdissection from a specimen according to claim 34, the method comprising the steps of:

pretreatment of the sample surface with solutions containing element with a specific surface affinity to desired targets as well as a specific surface affinity to the selectively activatable layer.

43. A method of laser capture microdissection from a specimen according to claim 42, the method comprising the steps of:

the pretreatment includes labeling with polymer microspheres (e.g., polystyrene latex spheres) attached to specific affinity tethers which recognize specific target molecules on the surface of the sample elements desired to be captured.

44. A method for non-contact laser capture microdissection from a visualized specimen, the method comprising the steps of:

providing a support for supporting and viewing the visualized specimen;

providing a supporting substrate;

placing a selectively activatable layer on the supporting substrate, which upon activation causes volumetric expansion with an extremity of the volumetric expansion exceeding a first interval taken substantially normal to a surface of the selectively activatable layer;

interconnecting the supporting substrate and the support to maintain the first surface at a spatial separation from all parts of the visualized specimen in juxtaposition with respect to the visualized specimen at the first interval of spatial separation from the visualized specimen;

locally activating the selectively activatable layer to bring the first surface into contact with the visualized specimen at pedestal of material to adhere to the selected portion of the specimen;

separating the selectively activatable layer to microdissect the selected portion of the specimen; and,

after the separating step, locally activating the selectively activatable layer to cause any pedestal protruding from the activatable layer to retract.

45. A method for non-contact laser capture microdissection from a visualized specimen according to claim 44, the method comprising:

utilizing a broader beam of radiation after the separating step to locally activate the selectively activatable layer to cause any pedestal protruding from the activatable layer to retract.

46. A method for non-contact laser capture microdissection from a visualized specimen according to claim 44, the method comprising:

utilizing a lower power beam of radiation after the separating step to locally activate the selectively activatable layer to cause any pedestal protruding from the activatable layer to retract.